

Application No. 09/914,708

Reply to Office Action

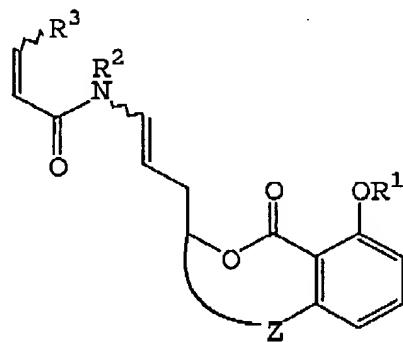
AMENDMENTS TO THE CLAIMS

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This listing of claims replaces all prior versions and listings of claims in the application.

JUL 18 2006

1. (Currently Amended) A method of treating ~~an intra-organellar acidification of intracellular organelles~~ ~~a condition treatable~~ by the inhibition of vacuolar-type (H⁺)-ATPase, said method comprising administering to a patient an amount effective to treat ~~intra-organellar acidification of intracellular organelles~~ ~~of a~~ inhibit vacuolar-type (H⁺)-ATPase of at least one compound of the formula:



(I).

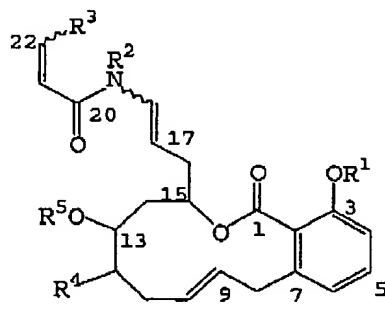
wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; the aromatic ring is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; the saturated alkyl, unsaturated alkyl and aryl substituents defined in R¹-R³ and R⁶ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and Z is a contiguous linker comprising a chain of 7-10 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR¹ and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 12-15 membered ring; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof, wherein the condition is selected from the group consisting of urinary acidification, bone resorption, osteoporosis, fertility, angiogenesis, glaucoma, and Alzheimer's disease.

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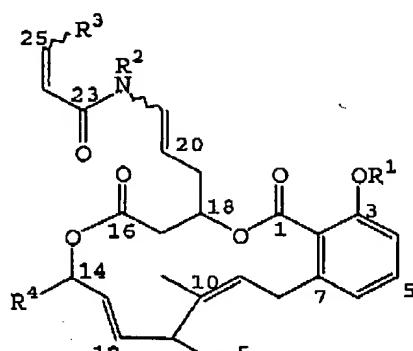
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2. (Canceled)

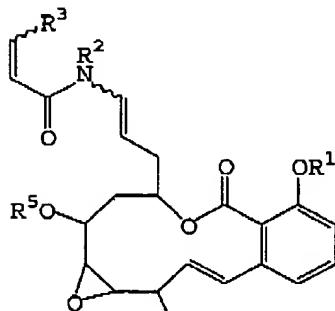
3. (Previously Presented) The method of claim 1, wherein said compound is selected from the group consisting of:



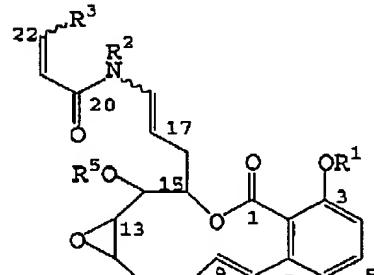
(IA),



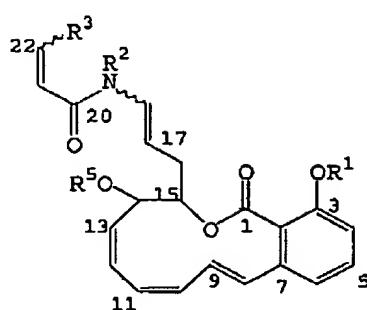
(IB),



(IC),



(ID),



and

(IE),

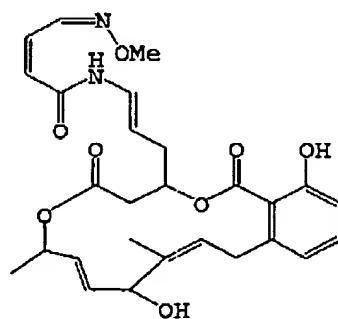
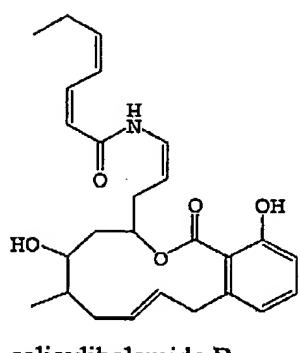
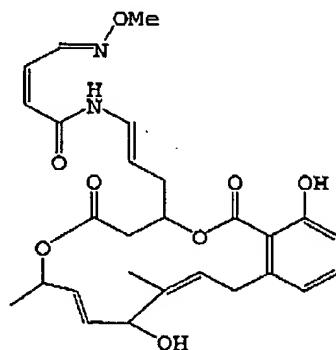
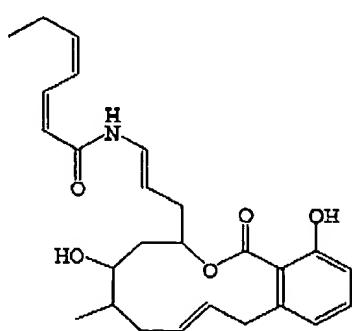
wherein R¹ and R² are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is H, a

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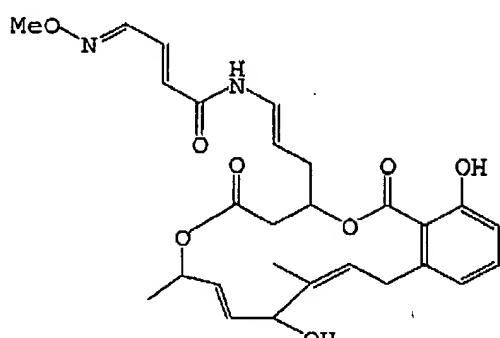
straight-chain or branched saturated or unsaturated alkyl, or an aryl; R³ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; R⁴ is H, an alkyl, or R⁷CH₂-, wherein R⁷ is R⁶O-, R⁶CO₂-, or R⁶SO₃-; R⁵ and R^{5'} are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R⁶CH₂-, R⁶CO-, or R⁶SO₂-; the saturated alkyl, unsaturated alkyl and aryl defined in R¹-R³, R⁵, R^{5'} and R⁶, and the alkyl defined in R⁴, are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and the aromatic ring of formula (I) is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof,

4. (Previously Presented) The method of claim 3, wherein said compound is selected from the group consisting of:

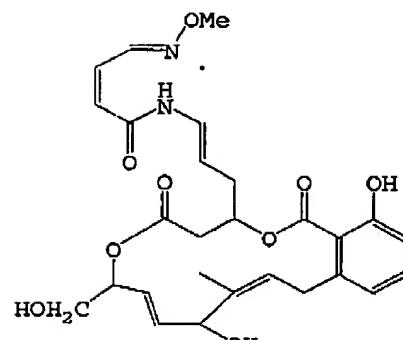


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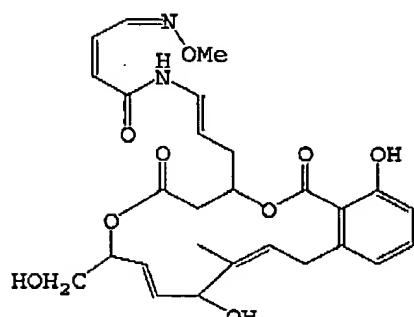
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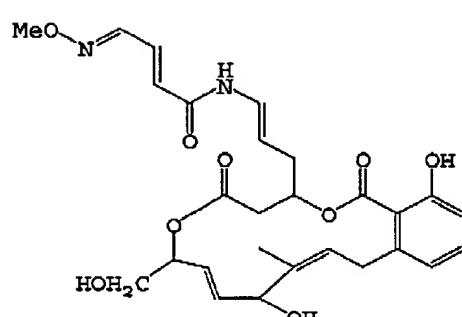
lobatamide C,



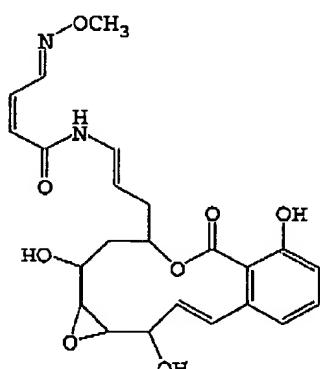
lobatamide D,



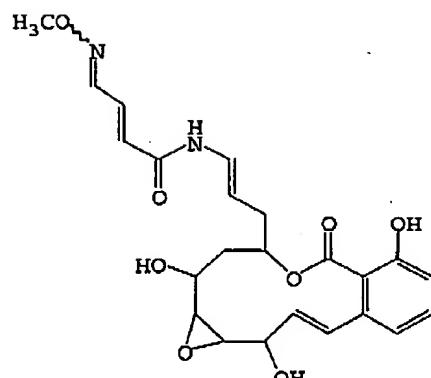
lobatamide E,



lobatamide F,



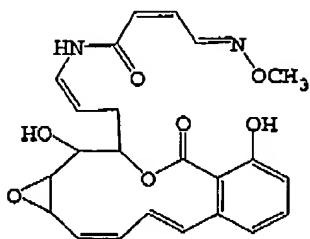
CJ-12,950,



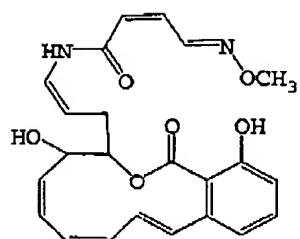
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oximidine 1, and

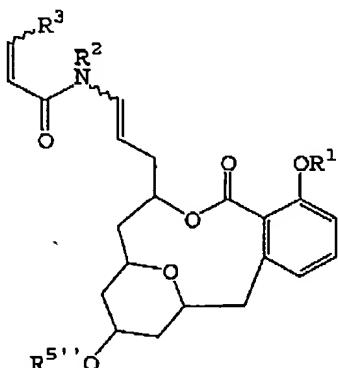


oximidine 2;

or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

5. (Canceled)

6. (Currently Amended) A method of treating ~~an intra-organellar acidification of intracellular organelles~~ ~~a condition treatable by the inhibition of vacuolar-type (H⁺)-ATPase~~, said method comprising administering to a patient an amount effective to ~~treat intra-organellar acidification of intracellular organelles of a~~ ~~inhibit~~ vacuolar-type (H⁺)-ATPase of at least one compound of the formula:



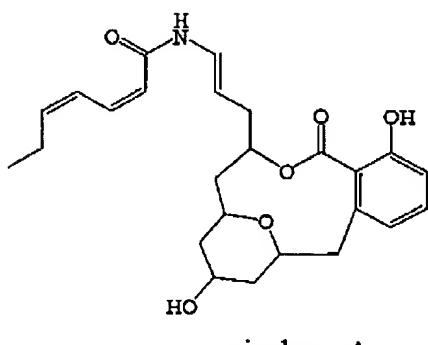
(IF),

wherein R¹-R³ are as defined in claim 1 and R^{5''} is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R⁶CH₂-, R⁶CO-, or R⁶SO₂-, wherein R⁶ is as defined in claim 1 and the saturated alkyl, unsaturated alkyl and aryl defined in R^{5''} are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano, wherein the condition is selected from the group consisting of urinary acidification, bone resorption, osteoporosis, fertility, angiogenesis, glaucoma, and Alzheimer's disease.

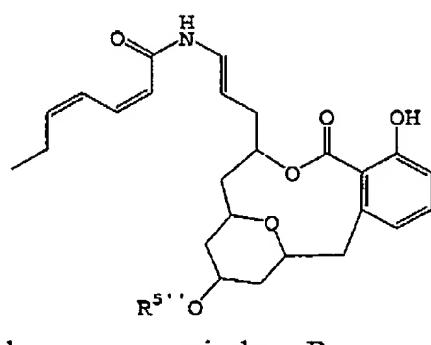
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7. (Previously Presented) The method of claim 6, wherein said compound is selected from the group consisting of:



apicularen A



apicularen B,

wherein R^{5''} is N-acetyl-β-D-glucosamine.

8. (Previously Presented) The method of claim 1, which further comprises co-administering to a patient in need thereof a therapeutically effective amount of at least one additional compound other than a compound defined in claim 1.

9. (Previously Presented) The method of claim 8, wherein said additional compound is selected from the group consisting of baflomycins and concanamycins.

10. (Previously Presented) The method of claim 9, wherein said additional compound is concanamycin A.

11. (Previously Presented) The method of claim 9, wherein said additional compound is baflomycin A₁.

12. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit intra-organellar acidification of intracellular organelles.

13. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit urinary acidification.

14. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit bone resorption.

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15. (Previously Presented) The method of claim 14, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to treat osteoporosis.

16. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit fertility.

17. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to inhibit angiogenesis.

18.-31. (Canceled)

32. (New) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to treat glaucoma.

33. (New) The method of claim 1, wherein said vacuolar-type (H⁺)-ATPase inhibiting-effective amount is effective to treat Alzheimer's disease.